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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	

ART UNIT	PAPER NUMBER
1633	

DATE MAILED: 11/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/530,539	ONO ET AL.	
	Examiner	Art Unit	
	Fereydoun G. Sajjadi	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/27/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: Notice to comply with sequene rules..

DETAILED ACTION

This action is in response to the preliminary amendment dated, amending claims 1-9. No new claims have been added and no claims have been cancelled.

Claims 1-9 are pending in the application and under current examination.

Objections to the Specification

The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

The specification is objected to for missing Figures referred to in the text of the disclosure, such as Figure 1, p. 12 and Figure 6, p. 17. The specification further appears devoid of any Figure legends for the missing Figures. The instant application is a 371 of PCT/FR03/03024, that contains six Figures relevant to the instant application. The instant application is thus entitled to a filing date. However, applicants are required to:

> (A) accept the application, as filed, without all of the drawing figure(s) referred to in the specification;
>
> (B) file any omitted drawing figure(s) with an oath or declaration in compliance with 37 CFR 1.63 and 37 CFR 1.64 referring to the omitted drawing figure(s) and a petition under 37 CFR 1.182 with the petition fee set forth in 37 CFR 1.17*>(f)<, requesting the date of submission of the omitted drawing figure(s) as the application filing date; or
>
> (C) file a petition under 37 CFR 1.53(e) with the petition fee set forth in 37 CFR1.17*>(f)< alleging that the drawing figure(s) indicated as omitted was in fact deposited with the USPTO with the application papers, including any and all evidence supporting the allegation. See MPEP § 503. The petition fee will be refunded if it is determined that the drawing figure(s) was in fact received by the USPTO with the application papers deposited on filing.
>
> If applicant is willing to accept the application, as filed, without all of the drawing figure(s) referred to in the application (item A above), applicant is required to submit (1) an amendment to the specification canceling all references to the omitted drawing figure(s) including any reference numerals shown only in the omitted drawing figure(s), (2) an amendment with replacement sheets of drawings in compliance with 37 CFR 1.121(d) renumbering the drawing figure(s) submitted on filing consecutively, and (3) a further amendment to the specification correcting references to drawing figure(s) to correspond with the relabeled

drawing figure(s), both in the brief and detailed descriptions of the drawings. The amendment should be submitted in response to the Office action. (See MPEP 601.01(g) A.)

If an application was filed on or after September 21, 2004, and contains a claim under 37 CFR **1.55** for priority of a prior-filed foreign application, or a claim under 37 CFR **1.78** for the benefit of a prior-filed provisional, nonprovisional, or international application that was present on the filing date of the application, and the omitted portion of the drawing(s) was inadvertently omitted from the application and is completely contained in the prior-filed application, applicant may submit an amendment to include the inadvertently omitted portion of the drawing(s) pursuant to 37 CFR **1.57**(a). The amendment should be submitted in response to the Office action and must comply with 37 CFR **1.57**(a) and 37 CFR **1.121**. See MPEP § **201.17**.<

Applicants are additionally required to provide a brief description of the drawing figure(s) in the specification.

Failure to Comply with Nucleotide and /or Amino Acid Sequence Disclosures 37CFR §1.821-1.825

37 CFR § 1.821 (d) states: Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application. The primer sequences recited in the specification, such as those on pages 11, 16, 20 and 22 do not include sequence identifiers.

A notice to comply with the sequence rule requirements has been included with this action. Applicant is required to check both the as filed paper and CRF sequence listings to ensure concordance with the sequences disclosed in the specification. If the primer sequences are present in the sequence listing as filed, the instant application may be placed in compliance with 37 CFR 1.821-1.825 by amending the specification to refer to the primer sequences by appropriate SEQ ID NOS.

Claim Objections

Claims 1-9 are objected to because of the following informalities: The independent claims lack the article "A" and the dependent claims lack the article "The" at the beginning of each claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. §112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: introduction of the transgene by microinjection into the fertilized embryo pronucleus and the implantation of said embryo into a pseudopregnant mouse; or the introduction of the transgene into mouse ES cells, and following homologous recombination in the ES cell genome, the ES cells are transferred by microinjection into the blastocyst of a fertilized embryo, said blastocyst is subsequently implanted into a pseudopregnant mouse.

Claim 1 recites the limitation "the extracellular domain of the nectin-1 or HveC" in the 5th and 6th lines of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim 1 is unclear in the recitation of the limitation "germinal transgenesis". As the instant specification fails to define this term, it may encompass production of transgenic animals by pronuclear microinjection of a fertilized embryo, or said production using ES cell transfer, or nuclear transfer, or in vivo transfer of genetic material to an egg via a sperm. Thus, the metes and bounds of "germinal transgenesis" remain undefined.

Claim 1 is unclear in reciting the limitation: "a transgene allowing the expression of a chimeric protein". While a promoter may drive the expression of an operably linked chimeric sequence, it is not clear how any transgene would allow the expression of a chimeric protein.

Claim 1 is further unclear in the recitation: "a chimeric protein composed on the one hand of the extracellular domain of the nectin-1...and on the other of the crystallisable fragment of an immunoglobulin". It is not clear if said handedness denotes a direct linkage of the two different proteins, or alternative structural variations of the two parts of the chimeric protein. Claims 4 and 8 contain the same limitation.

Claim 1 is further unclear in the recitation of "an appropriate system of expression". It is not clear what constitutes an "appropriate system". Thus, the metes and bounds of said appropriate system remain undefined. Claim 8 is similarly unclear.

Claim 3 is unclear. The claim is drawn to a process wherein the nectin-1, or HveC and/or immunoglobulin belong to the homologous species. It is not clear whether said proteins belong to any single species of mammal, or whether said proteins belong to the same species of mammal that is being produced by the process. Claim 4 is similarly unclear.

Claim 5 is unclear. The claim recites the limitation of a sub-part of the extracellular domain of nectin-1 or HveC. As the claim does not define any specific parts, it is not clear what a sub-part is representing. Thus the metes and bounds of sub-part remain undefined.

Claim 9 is unclear. The claim is directed to genetic material such as semen, or oocyte or embryo. While semen, oocytes and embryos contain genetic material, they are not themselves the genetic material, as claimed.

Claim 2 depends from claim 1, claims 6 and 7 depend from claim 4. Claims 2, 6 and 7 are therefore included in the rejection.

Claim Rejections - 35 USC § 112 – Written Description

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims embrace a large number of species of mammals, containing transgenes expressing numerous chimeric proteins containing parts or sub-parts of the extracellular domains of HveC and nectin-1. The specification fails to disclose any examples of the numerous mammalian species or the parts and sub-parts of nectin-1 or HveC proteins. The specification does not describe the structure or functional nature of any chimeric proteins containing parts or sub-parts of nectin-1 or HveC from numerous species of animals. The specification only discloses the chimeric proteins containing the extracellular domain of Hvem (specifically, the mouse and porcine HveC) fused to the Fc portion of the human immunoglobulin IgG-1, introduced into the fertilized mouse embryo pronuclei (pp. 11 and 16).

In addition to numerous species of animals, the claims encompass a large number of possible peptide parts or derivatives of HveC and nectin-1 from a multitude of species, and thus constitute a claimed genus that encompasses peptides yet to be discovered. The specification fails to disclose any additional transgenic species of animals, or species of nectin-1 or peptide parts, sub-parts or derivatives of HveC, or provide a description for any structural features of modified forms of the claimed genus. As such, the Artisan of skill could not predict that Applicant possessed any species of mammals, or nectin-1 or parts of HveC, other than mouse and porcine HveC expressed in mice..

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail such that the Artisan can reasonably conclude that the inventor(s) had possession of the claimed invention. Such possession may be demonstrated by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and/or formulae that fully set forth the claimed invention. Possession may be shown by an actual reduction to practice, showing that the invention was "ready for patenting", or by describing distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention (January 5, 2001 Fed. Reg., Vol. 66, No. 4, pp. 1099-11). Moreover, MPEP 2163 states:

> [A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

Applicant's attention is also directed to *In re Shokal*, 113 USPQ 283 (CCPA 1957), wherein it is stated:

> It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. *In re Soll*, 25 CCPA (Patents) 1309, 97 F2d 623, 38 USPQ 189; *In re Wahlforss*, 28 CCPA (Patents) 867, 117 F2d 270, 48 USPQ 397. The decisions do not however fix any definite number of species which will establish completion of a generic invention and it seems evident therefrom that such number will vary, depending on the circumstances of particular cases. Thus, in the case of small genus such as the halogens, consisting of four species, a reduction to practice of three, perhaps even two, might serve to complete the generic invention, while in the case of a genus comprising hundreds of species, a considerably larger number of reductions to practice would probably be necessary.

Overall, what these statements indicate is that the Applicant must provide adequate description of such core structure and function related to that core structure such that the Artisan of skill could determine the desired effect. Hence, the analysis above demonstrates that Applicant has not determined the core structure for full scope of the claimed genus.

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. Therefore, the breadth of the claims as reading on numerous species of transgenic mammals expressing chimeric forms of nectin-1 or HveC proteins, or a multitude of their parts and sub-parts yet to be discovered; in view of the level of knowledge or skill in the art at the time of the invention, an Artisan of skill would not recognize from the disclosure that Applicant was in possession of the genus of transgenic mammals or the transgenes encoding either nectin-1 or parts of nectin-1 and HveC. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

In conclusion, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that Applicant is in possession of numerous transgenic animals or the transgenes expressing chimeric nectin-1 from a large number of species, or numerous parts or fragments of nectin-1 and HveC, at the time the application was filed. Thus it is concluded that the written description requirement is not satisfied for the claimed genus.

35 USC § 112-Lack of Enablement

Claims 1-9 are rejected under 35 U.S.C.§112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for a process for producing any non-human animal rendered resistant by germinal transgenesis to an infection by any alphaherpesvirus, wherein a transgene allowing the expression of a chimeric protein composed of the extracellular domain of nectin-1 or HveC or one of its parts and a crystallizable portion of an immunoglobulin, is introduced by insertion or homologous recombination, or transgenic mammals produced by said processes, as claimed.

This rejection is based on two (2) separate issues: **1)** the absence of an enabling disclosure for the production of numerous transgenic non-human animals or the generation of said transgenic animals by homologous recombination and **2)** the absence of an enabling disclosure for the production of transgenic animals expressing fusion proteins of nectin-1 or its parts, or parts of HveC, as claimed. In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by Applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404:

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

MPEP § 2164.04 states: "[W]hile the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection."

As a first issue **(1)**, the specification does not provide an enabling disclosure for the production of numerous transgenic non-human animals or the generation of said transgenic animals by homologous recombination.

The specification states that infection mediator abilities of HveC in relation to the entry of the targeted virus, so as to ultimately inhibit the entry of this virus into the cell and favor its elimination, is by a process which is still to be determined (p. 7). The specification discloses the generation of mice by pronuclear microinjection of transgenes comprising the extracellular domain of the murine HVEM receptor (p. 11) or the porcine HVEM receptor (pp. 15-16) and the Fc portion of human IgG-1, to generate several transgenic mouse lines. The specification is silent on the introduction of said transgenes by homologous recombination into a targeted chromosomal location. Tables 1-4 disclose data from the various transgenic lines, showing different concentrations of mouse HVEM-Ig in the serum of the mice, with 3 of the 4 lines with the highest HVEM-Ig concentration showing resistance to HSV-1 intravenous virus infection (p. 13). However, the mice were not protected against infection by PRV virus (p. 14), thus suggesting the presence of tropism for different alphaherpesviruses.

Table 6 discloses results from transgenic mice expressing a porcine HVEM-Ig transgene, wherein viral challenge by intra-peritoneal injections of PRV virus resulted in the survival of the mice (p. 17), but survival was reduced to 70% when virus was introduced intranasally (Table 7 and pp. 17-18). The specification is absent any data from the intravenous administration of PRV to these mice.

Therefore, the data suggest that the route of infection likely plays a role in the degree of resistance to viral infection, though the mechanism of said resistance remains unknown. Further, resistance to infection appears to be dependent on both the type of HveC receptor and the particular alphaherpesvirus. As the specification fails to disclose either a transgenic bovine or a transgenic porcine expressing an HveC fusion protein, any resistance of these transgenic animals to PRV or BHV-1 virus infections remains unknown and would have to be determined by further experimentation. Moreover, the prior art of Mullins et al. (J. Clin. Invest 98:1557-1560; 1996), discloses that "the use of non-murine species for transgenesis will continue to reflect the suitability of a particular species for the specific questions being addressed, bearing in mind that a given construct may react very differently from one species to the another." (summary, p. 1559). Additionally, Machaty et al. (Cloning & Stem Cells 4:21-27, 2002) in addressing pronuclear microinjection, state: "during microinjection, several copies of the gene sequence are microinjected into the pronuclei of the zygotes, where they can integrate into one or more of the

host chromosomes, at an early stage of development...The integration of the injected DNA occurs at random, and the number of copies inserted cannot be controlled...the expression of the foreign gene...is greatly affected by the integration site...resulting in mosaic embryos...[that] cannot transmit the transgene to progeny" (first column, p. 22). Therefore, the prior art highlights the unpredictability in generating transgenic animals by pronuclear microinjection of transgenes.

Regarding the claimed limitation of introducing the transgenes by homologous recombination in the genome, no such guidance is provided by the specification. For homologous recombination at a predetermined site, sequence homologies flanking the transgene to be introduced must be provided. However, no such sequences have been disclosed, and as such the person of skill in the art, would not know to which chromosomal location the transgene must be homologously recombined or targeted. Further, the generation of transgenic animals by homologous recombination of transgenes, necessitates the use of ES cells, that while proven in mice, have not been developed in other animals, such as pigs (Machaty et al., second column, p 22).

The instant claims encompass a process for producing a non-human mammal by germinal transgenesis. The specification does not define the term "germinal transgenesis" and only discloses that "Pronuclear microinjection of the DNA segment encoding the transgene or nuclear transfer of cells transformed in culture by the transgene in particular can be used." (p. 10). The instant specification does not provide any guidance for nuclear transfer to any non-human mammal (a procedure that remains unpredictable and is not considered routine in the art, as disclosed by Machaty et al. (entire disclosure)). Therefore, when given the broadest reasonable interpretation, the instant claims embrace the introduction of a transgene into a germ cell, such as a sperm i*n vitro*, or *in vivo*. The instant disclosure provides no such guidance, and the prior art is silent on the introduction of a transgene into a sperm cell for the production of transgenic animals. The process of germinal transgenesis thus would require further undue experimentation on the part of the skilled Artisan to determine its efficacy.

As a second issue **(2)**, the specification does not provide an enabling disclosure for the production of transgenic animals expressing fusion proteins of nectin-1 or its parts, or parts of HveC. The instant specification discloses mice expressing fusions proteins comprising the extracellular domain of the murine HVEM receptor (HveC, p. 11) or the porcine HVEM receptor

(HveC, pp. 15-16) and the Fc portion of human IgG-1. The specification fails to disclose any information or results for fusion proteins comprising the extracellular domain of nectin-1 or parts or sub-parts of HveC, or nectin-1.

As the specification is silent on the structural elements required for receptor mediated infection of alphaherpesviruses via parts or sub-parts of nectin-1 and HveC, and given the unpredictabilities of transgenic mice expressing even the full HveC polypeptide, as observed in the instant specification and addressed in the foregoing, the person of skill in the art would not be able to predict the result of expressing either nectin-1 or parts and sub-parts of nectin-1 or HveC in a transgene fusion product in numerous transgenic animals, and their respective abilities to render the animals resistant to alphaherpesvirus infection.

The guidance provided by the specification amounts to an invitation for the skilled Artisan to try and follow the disclosed instructions to make and use the claimed invention. The specification merely discloses transgenic mice expressing chimeric HveC/Fc IgG protein, produced by pronuclear microinjection into fertilized embryos. The detail of the disclosure provided by Applicant, in view of the prior art, must encompass a wide knowledge, so that the Artisan of skill would be able to practice the invention as claimed by Applicant, without undue burden being imposed on such Artisan. This burden has not been met because it would require undue experimentation to effectively produce numerous transgenic animals rendered resistant to alphaherpesvirus infection by transgenesis by insertion or homologous recombination of transgenes encoding fusion proteins of nectin-1 or parts and sub-parts of nectin-1 and HveC, as claimed in the instant application.

Therefore, in view of the art recognized high level of unpredictability in the art of producing transgenic animals other than mice, and the methods encompassed by germinal transgenesis, together with the large quantity of research required to define these unpredictable variables, and the lack of guidance provided in the specification regarding the structure and function of nectin-1 or its parts and sub-parts, or parts and sub-parts of HveC, it is the position of the examiner that it would require undue experimentation for one of skill in the art to practice the invention claimed. Hence, absent a strong showing by Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. §103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. §103(c) and potential 35 U.S.C. §102(e), (f) or (g) prior art under 35 U.S.C. §103(a).

To the extent that claims 1-5 are enabled for transgenic mice rendered resistant to an infection by an alphaherpesvirus, said mice containing a transgene encoding a chimeric HveC/Fc IgG fusion protein, and a process of producing said mice, the following rejection over the prior art is applicable:

Claims 1-5 are rejected under 35 U.S.C. §103(a) as being unpatentable over Fiume et al. (U.S. Patent No.: 6,469,155, filed Nov. 9, 1999), in view of Bujard et al. (US. Patent No.: 5,866,755, Feb. 2, 1999).

Fiume et al. state that alphaherpesviruses include HSV-1, HSV-2, PRV, and BHV-1 infect a variety of cells (column 1) and describe various fusion proteins between various segments of HIgR (herpesvirus immunoglobulin-like receptor) and the Fc portion of human IgG1 (Abstract and column 4). The authors teach that HIgR, and/or its splice variant HveC, are involved in cell to cell spread of HSV (column 3, last paragraph). Specifically described are sVCC(PVRα)-Fc containing the soluble V domains of HIgR (column 4 and Example 4), in addition to the discovery in the prior art that a soluble form of HveC containing the entire ectodomain is capable of such binding (column 17). Fiume et al. further state that an object of their invention is to provide cells that are resistant to infection by HSV-1, HSV-2 and BHV-1 (column 1). Fiume et al. state that an embodiment of their invention is the construction of transgenic mice expressing the alphaherpesvirus receptors that mediate HSV and BHV-1 entry, from transgenes to produce a mouse model system for the viral infections (column 3); thus

providing the motivation to use their constructs as transgenes in transgenic mice.

Bujard et al. describe transgenic animals carrying a transgene comprising a nucleic acid molecule encoding a fusion protein composed of two polypeptides (Abstract). The authors describe the creation of a transgenic animal by introducing a nucleic acid encoding the fusion protein (linked to appropriate regulatory elements) into the male pronuclei of fertilized oocytes by microinjection and allowing the oocytes to develop in a pseudopregnant female foster animal. Additionally stating that methods for generating transgenic animals such as mice have become conventional in the art (column 15). The generation of mice expressing a fusion protein is set forth in Example 6. Therefore, a person of ordinary skill in the art would have been motivated to combine the teachings of Fiume et al. and Bujard et al. to produce transgenic mice expressing the HveC-Fc fusion protein. A person of ordinary skill in the art, having combined the HveC-Fc construct of Fiume et al. as a transgene, with the method of generating transgenic mice expressing a fusion protein as taught by Bujard et al., would be able to practice the instantly claimed method, resulting in the claimed transgenic animal of the instant invention, said transgenic animal further capable of expressing an alphaherpesvirus receptor, with a reasonable expectation of success.

Thus it would have been *prima facie* obvious for a person of ordinary skill in the art, to combine the fusion protein construct of Fiume et al. with the transgenic mouse generation method of Bujard et al. at the time of the instant invention.

Conclusion

Claims 1-9 are not allowable.

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst William Phillips, whose telephone number is **(571) 272-0548**. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00 am-4:00 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on **(571) 272-0731**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of

such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

For all other customer support, please call the USPTO Call Center (UCC) at **(800) 786-9199**.

Fereydoun G. Sajjadi, Ph.D.
Examiner, USPTO, AU 1633

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER

Notice to Comply	Application No. 10/530,539	Applicant(s) Ono et al.	
	Examiner Fereydoun Sajjadi	Art Unit 1633	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e). Therefore a search of the correct sequence is not possible.

☒ 7. Other: The specification contains nucleotide sequences without SEQ ID NO identifiers.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
PatentIn Software Program Support
Technical Assistance.....703-287-0200
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APPLICATION NO./CONTROL NO.	FILING DATE	FIRST NAMED INVENTOR / PATENT IN REEXAMINATION	ATTORNEY DOCKET NO.
10/530,539	09/19/2005	Etsuro Ono	HER0071

EXAMINER	
Fereydoun G. Sajjadi	
ART UNIT	**PAPER**
1633	

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. There are no sequence identifiers for the sequences listed throughout the specification. Applicant is required to thoroughly review the specification and comply with all sequence rules. For example, the following sequences in the specification do not have sequence identifiers: page 69 line 26, page 70 line 4, page 79 line 25, page 85, line 3 and 4 and figure 7.

Applicant is given ONE MONTH, or THIRTY DAYS, whichever is longer, from the mailing date of this letter within which to comply with the sequence rules, 37 CFR 1.821 - 1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR 1.821(g). Extensions of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR 1.136(a). In no case may an applicant extend the period for reply beyond the SIX MONTH statutory period. Direct the reply to the undersigned. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is **(571) 272-3311**. The examiner can normally be reached Monday through Friday, between 7:00 am-4:00 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave T. Nguyen can be reached on **(571) 272-0731**. The fax phone number for the organization where this application or proceeding is assigned is **(571) 273-8300**. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Fereydoun G. Sajjadi, Ph.D.
Examiner, Art Unit 1633